P29690.P05

GREENBLUM & BERNSTEIN, P.L.C.
Intellectual Property Causes
1950 Roland Clarke Place
Reston, VA 20191
(703) 716-1191

Mail Stop Appeal Brief-Patents
Confirmation No. 3976

In re application of : Ghita LANZENDORFER et al.
Attorney Docket No. P29690

Application No. : 08/849,525
Group Art Unit : 1617

Filed : August 29, 1997
Examiner : Cotton, Abigail Manda

For : USE OF FLAVONOIDS AS IMMUNOMODULATING OR IMMUNO-PROTECTIVE AGENTS IN COSMETIC AND DERMATOLOGICAL PREPARATIONS

Mail Stop Appeal Brief-Patents
Commissioner for Patents
U.S. Patent and Trademark Office
Customer Service Window, Mail Stop Appeal Biref-Patents
Randolph Building
401 Dulany Street
Alexandria, VA 22314

Sir:

Transmitted herewith is an **Appeal Brief Under 37 C.F.R. §41.37** in the above-captioned application.

____ Small Entity Status of this application under 37 C.F.R. 1.9 and 1.27 has been established by a previously filed statement.

____ A Request for Extension of Time.

____ No additional fee is required.

The fee has been calculated as shown below:

Claims After Amendment	No. Claims Previously Paid For	Present Extra	Small Entity		Other Than A Small Entity	
			Rate	Fee	Rate	Fee
Total Claims: 20	*20	0	x25=	$	x 50=	$ 0.00
Indep. Claims: 2	**3	0	x100=	$	x200=	$ 0.00
Multiple Dependent Claims Presented			+180=	$	+360=	$ 0.00
Extension Fees for ____ Month(s)				$		$ 0.00
Appeal Brief Filing Fee						$500.00
* If less than 20, write 20 ** If less than 3, write 3			Total:	$	Total:	$500.00

____ Please charge my Deposit Account No. 19-0089 in the amount of $_____.

__X__ A check in the amount of $500.00 to cover the filing fee is included.

__X__ The U.S. Patent and Trademark Office is hereby authorized to charge payment of the following fees associated with this communication or credit any overpayment to Deposit Account No. 19-0089.

__X__ Any additional filing fees required under 37 C.F.R. 1.16.

__X__ Any patent application processing fees under 37 C.F.R. 1.17, including any required extension of time fees in any concurrent or future reply requiring a petition for extension of time for its timely submission (37 C.F.R. 1.136(a)(3)).

Heribert F. Muensterer
Reg. No. 50,417

Neil F. Greenblum
Reg. No. 28,394

P29690.A08

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicant : Ghita LANZENDORFER et al.

Confirmation No. 3676
Group Art Unit: 1617

Serial No. : 08/849,525

Examiner: Cotton, Abigail Manda

Filed : August 29, 1997

For : USE OF FLAVONOIDS AS IMMUNOMODULATING OR IMMUNOPROTECTIVE AGENTS IN COSMETIC OR DERMATOLOGICAL PREPARATIONS

APPEAL BRIEF UNDER 37 C.F.R. § 41.37

Commissioner for Patents
U.S. Patent and Trademark Office
Customer Service Window, Mail Stop Appeal Brief - Patents
Randolph Building
401 Dulany Street
Alexandria, VA 22314

Sir:

This Appeal is from the Examiner's Final Rejection of claims 37-56 set forth in the Final Office Action mailed from the U.S. Patent and Trademark Office on September 13, 2006.

A Notice of Appeal and a Pre-Appeal Brief Request for Review in response to the September 13, 2006 Final Office Action and the Advisory Action mailed November 22, 2006 were filed on December 11, 2006.

The requisite fee under 37 C.F.R. § 41.20(b)(2) for filing this Appeal Brief ($500.00) is being paid by the enclosed check.

Inasmuch as this Appeal Brief is being filed within the one-month period from the mailing date of the Notice of Panel Decision from Pre-Appeal Brief review mailed January 19, 2007, set to expire on February 20, 2007 (February 19, 2007 being a Federal Holiday), it is believed that no extension of time is required. However, the Patent and Trademark Office is hereby authorized to

charge any fee necessary for maintaining the pendency of this application, including any appeal or extension of time fees that may be necessary, to Deposit Account No. 19-0089.

TABLE OF CONTENTS

I. REAL PARTY IN INTEREST

The real party in interest in this appeal is Beiersdorf AG of Hamburg, Germany. The assignment was recorded in the U.S. Patent and Trademark Office on December 10, 1997 at REEL 8826, FRAME 0738.

II. RELATED APPEALS AND INTERFERENCES

Appellants, Appellants' representative or the Assignee are not aware of any other prior and pending appeals, interferences or judicial proceedings which may be related to, directly affect or be directly affected by or have a bearing on the Board's decision in the pending appeal.

III. STATUS OF CLAIMS

The status of the claims is as follows:

Claims 37-56 are pending in this application. Claims 1-36 are cancelled.

Each of claims 37-56 is indicated as rejected in the Final Office Action mailed September 13, 2006. (It is noted that the Notice of Panel Decision from Pre-Appeal Brief Review mailed January 19, 2007 mentions only claims 37, 38, 43 and 48-50. It is assumed that this is due to an oversight. Claims 39-42, 44-47 and 51-56 have never been cancelled and are thus, still pending).

The rejection of each of claims 37-56 is under appeal. Claims 37-56 involved in the appeal are reproduced in the Claims Appendix attached hereto.

IV. STATUS OF AMENDMENTS

No Amendment has been filed subsequent to the Final Office Action mailed September 13, 2006.

V. SUMMARY OF CLAIMED SUBJECT MATTER

A. Claim 37

Independent claim 37 is drawn to a method of treating or modulating immunosuppression of skin cells induced by UVB radiation. The method comprises topically applying to the skin of a person in need thereof an effective amount therefor of a cosmetic or dermatological formulation which comprises one or more flavonoids selected from alpha-glucosylrutin, alpha-glucosylmyricitrin, alpha-glucosylquercitrinin, alpha-glucosylquercitrin, quercetin, rutin, chrysin, kaempferol, myricetin, rhamnetin, apigenin, luteolin, naringin, hesperidin, naringenin, hesperitin, morin, phloridzin, diosmin, fisetin, vitexin, neohesperidin, dihydrochalcone, flavone and genistein.

See, e.g., page 5, line 30 to page 6, line 7 and page 6, lines 10-14 in combination with page 8, lines 13-17 and page 9, lines 14-22, as well as page 31, lines 2-27 of the present application.

B. Claim 55

Independent claim 55 is drawn to method of treating immunosuppression of skin cells induced by UVB radiation. The method comprises topically applying to the skin of a person in need thereof an effective amount therefor of a cosmetic or dermatological formulation comprising (i) one or more flavonoids selected from alpha-glucosylrutin, alpha-glucosylmyricitrin, alpha-glucosylquercitrinin, alpha-glucosylquercitrin, quercetin, rutin, chrysin, kaempferol, myricetin, rhamnetin, apigenin, luteolin, naringin, hesperidin, naringenin, hesperitin, morin, phloridzin, diosmin, fisetin, vitexin, neohesperidin, dihydrochalcone, flavone and genistein, (ii) one or more cinnamic acid derivatives and (iii) one or more antioxidants.

See, e.g., page 5, line 30 to page 6, line 7 and page 6, lines 10-14 in combination with page 8, lines 13-17 and page 9, lines 14-22, as well as page 13, lines 1-6 and 24-28 and page 31, lines 2-27 of the present application.

VI. GROUNDS OF REJECTION TO BE REVIEWED ON APPEAL

The broad issues under consideration are:

1. Whether claims 37, 38, 43 and 48-50 are properly rejected under 35 U.S.C. § 103(a) as allegedly being unpatentable over Evans et al., U.S. Patent No. 5,358,752 (hereafter "EVANS") in view of Suzuki et al. U.S. Patent No. 5,145,781 (hereafter "SUZUKI") and as evidenced by *Harrison's Principles of Internal Medicine*, 1994, New York, McGraw-Hill, Inc., 13th ed., pp. 309-313 (hereafter "HARRISON").

2. Whether claims 39-43, 44-47, 51-53, 55 and 56 are properly rejected under 35 U.S.C. § 103(a) as allegedly being unpatentable over EVANS in view of SUZUKI as evidenced by HARRISON and further in view of N'GUYEN et al., U.S. Patent No. 5,023,235 (hereafter "N"GUYEN I").

3. Whether claim 54 is properly rejected under 35 U.S.C. § 103(a) as allegedly being unpatentable over EVANS in view of SUZUKI as evidenced by HARRISON and further in view of N'GUYEN et al., U.S. Patent No. 5,114,716 (hereafter "N"GUYEN II").

VII. ARGUMENTS

A. Summary of Rejections of Record

1. All claim rejections under 35 U.S.C. § 103(a) set forth in the final Office Action of September 13, 2006 are based on at least EVANS in view of SUZUKI as evidenced by HARRISON.

The rejection essentially alleges that EVANS teaches the topical application to skin of a composition comprising an antioxidant to control the oxidative damage of skin caused by UV radiation and that SUZUKI teaches that alpha-glycosylrutin (which comprises alpha-glucosylrutin) has properties as an antioxidant and is a UV absorbent and can be provided in pharmaceuticals and cosmetics, which allegedly renders it obvious to use a flavonoid such as alpha-glucosylrutin in the topical compositions of EVANS. The rejection concedes that EVANS and SUZUKI do not specifically teach applying an antioxidant to the skin of a patient that is in need of treatment or modulation of the immunosuppression of skin cells induced by UVB radiation. In this regard, the rejection relies on HARRISON which teaches that excessive exposure to UVB radiation is implicated in the development of a number of skin disorders, including the immunosuppression of skin cells. As far as Appellants can gather from the Examiner's corresponding comments, the Examiner appears to take the position that in view thereof, applying the composition of EVANS which is supplemented by the alpha-glycosylrutin of SUZUKI to sunburned skin "which has been exposed to excessive UVB radiation, and which is thus likely to have immunosuppression of the skin cells" will have the inherent effect of treating immunosuppression of the skin cells, thus allegedly rendering obvious the subject matter of claims 37, 38, 43 and 48-50.

2. With respect to the rejection of dependent claims 39-43, 44-47, 51-53, 55 and 56 the Examiner concedes that EVANS, SUZUKI and HARRISON do not specifically teach applying a composition that further comprises a cinnamic acid derivative, providing an antioxidant that is tocopherol or its derivatives or providing the composition in the form of an emulsion. In view thereof, the Examiner relies on N'GUYEN I and asserts that this document teaches that caffeic acid and its esters as well as tocopherols are known to have antioxidant activity and that caffeic acid can suitably be incorporated into cosmetic compositions. Regarding claims 51 and 52, the rejection

alleges that EVANS and SUZUKI teach suitable amounts of antioxidants such as flavonoid and caffeic acid in a cosmetic composition and that one of ordinary skill in the art would allegedly have found it obvious to vary and/or optimize the amounts and/or ratios of antioxidants provided in the composition, according to the guidance allegedly provided by the cited documents, to provide a composition having the desired properties. Regarding claim 53, the rejection alleges that N'GUYEN I teaches providing water-in-oil emulsions as carriers for cosmetics. Regarding claim 55, the rejection alleges that EVANS, SUZUKI and HARRISON teach the claimed method of treating skin by applying a flavonoid, and also allegedly teach that the composition can comprise another oxidant, such as rutin, wherefore it would allegedly have been obvious to incorporate the caffeic acid of N'GUYEN I into the method of EVANS, SUZUKI and HARRISON.

3. Regarding dependent claims 54 the rejection concedes that EVANS, SUZUKI and HARRISON do not specifically teach a gel as an example of a cosmetically acceptable carrier. In this regard, the rejection relies on N'GUYEN II which allegedly teaches that gels are known as cosmetically acceptable carriers for cosmetics.

B. Citation of Authority

To establish a *prima facie* case of obviousness, three basic criteria must be met. First, there must be some suggestion or motivation, either in the references themselves or in the knowledge generally available to one of ordinary skill in the art, to modify the reference or to combine reference teachings. Second, there must be a reasonable expectation of success. Finally, the prior art references must teach or suggest all the claim limitations. The teaching or suggestion to make the claimed combination and the reasonable expectation of success must both be found in the prior art, and not based on applicant's disclosure. In re Vaeck, 947 F.2d 488, 20 USPQ2d 1438 (Fed. Cir. 1991) and

MPEP 2142. "If the Examiner fails to establish a *prima facie* case, the rejection is improper and will be overturned." In re Rijckaert, 9 F.3d, 1532, 28 U.S.P.Q.2d, 1956 (Fed. Cir. 1993), citing In re Fine, 837 F.2d 1071, 1074, 5 U.S.P.Q.2d 1596, 1598 (Fed. Cir. 1988).

The appropriate starting point for a determination of obviousness is stated in Graham v. John Deere Co., 383 U.S. 1, 17, 148 U.S.P.Q. 459, 466 (1966):

> Under § 103, the scope and content of the prior art are to be determined; differences between the prior art and the claims at issue are to be ascertained and the level of ordinary skill in the pertinent art resolved. Against this background, the obviousness or nonobviousness of the subject matter is determined.

The test of obviousness *vel non* is statutory and requires a comparison of the claimed subject matter as a whole with the prior art to which the subject matter pertains. In re Brouwer, 77 F.3d, 422, 37 U.S.P.Q. 2d 1663 (Fed. Cir. 1996); In re Ochiai, 71 F.3d 1565, 37 U.S.P.Q. 2d 1127 (Fed. Cir. 1995). Obviousness can only be established by combining or modifying the teachings of the prior art to produce the claimed invention where there is some teaching, suggestion or motivation to do so found either explicitly or implicitly in the references themselves or in the knowledge generally available to one of ordinary skill in the art. MPEP 2143.01.

C. Independent Claim 37 is Not Properly Rejected under 35 U.S.C. § 103(a) as Being Unpatentable Over EVANS in View of SUZUKI as Evidenced by HARRISON

1. EVANS Fails to Provide Motivation to Incorporate an Antioxidant Different from Those Disclosed Therein into the Compositions Described Therein

EVANS teaches a skin care composition which contains an antioxidant effective amount of a phenolic diterpene compound of the ferruginol type and reduces the accumulation of lipid peroxides and other biological oxidation products in the skin, thereby being an effective agent against the production of peroxides in the skin resulting from sunlight, heat, radiation and the aging process. See Abstract of EVANS.

At column 1, lines 30-57 EVANS states (emphases added):

> The use of antioxidants to inhibit peroxidation is well known. The Cosmetic, Toiletry and Fragrance Association Inc. lists a nun%her [*sic*, number] of substances used as antioxidants in cosmetic formulations (CTFA Cosmetic Ingredient Handbook, 1st. Ed., 1988). These substances include the natural products ascorbic/erythorbic acids and related compounds, and tocopherols; as well as BHA, BHT, hydroquinone and other synthetic compounds. However, the CTFA Handbook describes the purpose of these antioxidants as follows: "Antioxidants are ingredients employed in cosmetics to prevent or retard spoilage from rancidity (or deterioration from reaction with oxygen). Antioxidants play a vital role in maintaining the quality, integrity, and safety of cosmetic products." Hence, the use of antioxidants in cosmetic products as generally practiced is targeted at maintaining the stability of the cosmetic ingredients themselves.
>
> Clearly, it is desirable to provide antioxidants in skin care products for the control of peroxidation in the skin tissue itself. It is particularly desirable to provide a means for controlling peroxide formation in skin exposed to sunlight having a harmful intensity of UVB radiation. The market for the sun care category of cosmetics is estimated at $450 million annually in the USA. Such cosmetic products are based on the use of agents which block out UVB and other types of potentially harmful radiation.

Further, in the passage from column 2, line 1, to column 3, line 2, EVANS states (emphases added):

> Nguyen et al., U.S. Pat. No. 5,017,397, disclose methods for the extraction of antioxidants from the Labiatae family of domestic spices including rosemary and sage. These extracts comprise typically 25% to 35% of the naturally occurring phenolic diterpene, carnosic acid. The antioxidant properties of carnosic acid are well documented, e.g. Brieskorn and Domling, Zeitschrift fur Lebensmitteluntersuchung und -forschung 141(1):10, 1969, and Schuler P., Food Antioxidants, Hudson B. J. F. Ed., Elsevier Pub., 1990, the latter showing that the antioxidant properties of carnosic acid are enhanced in the presence of ascorbate.
>
> Unfortunately, the Labiatae extracts of Nguyen et al. and others, contain carnosic acid in combination with unknown compounds. Unknown components may render the extracts unsuitable for use in human skin care applications. For example, such extracts invariably contain color and odor components which are incompatible with cosmetic products. The protection of skin tissue from peroxidation is a health care matter, so protective materials must be in pure compound form so that effectiveness and human safety can be assured through reproducible formulations.
>
> The present inventors have purified camosic acid from Labiatae spice extracts through a series of selective solubilizations and precipitations in aqueous ethanol/methanol solutions and liquid column chromatography. Carnosic acid so obtained has a 99%+purity. Pure carnosic acid can be oxidised to obtain the naturally occurring oxidative by-product, carnosol. [...]
>
> As demonstrated herein, these pure compounds are extremely effective in protecting the skin from peroxidation when applied topically. Carnosic acid, alkyl esters of carnosic acid, and carnosol are oil soluble, and thus, suited to inclusion in suntan oils, while sodium carnosate is soluble in water making it suitable for use in moisturizers and aqueous lotions. The compounds are freely soluble in propylene glycol, a standard cosmetic skin care solvent. The compounds are non-toxic for the use intended and have been fed to young mice at rates of 25, 50 and 75 mg/kg body weight without damage to growth or reproductive ability. The compounds are stable to expected heat exposure and are stable to high doses of UVB radiation. Furthermore, the documented synergism with ascorbate has been shown

by the inventors to be a direct result of the protection afforded by ascorbate to the compound during the antioxidant activity.

Accordingly, the invention provides a composition for use on skin, comprising an antioxidant effective amount of a pure phenolic diterpene compound of the ferruginol type which is dissolved or dispersed in a skin compatible carrier. The composition provides a temporary prophylactic effect against the production of peroxides in skin tissues to which it has been applied. Preferred phenolic diterpenes for use in the composition are camosic acid, a C_{1-5} alkyl ester of carnosic acid, carnosol, and carnosic acid alkali metal salts.

At column 4, lines 7-15, EVANS additionally states (emphasis added):

The diterpene antioxidants may be combined with ascorbic acid or related compounds such as erythorbic acid, their alkali metal salts, to provide a synergistic antioxidation effect. Preferably, the ascorbic or erythorbic acid or salt is added to the composition in an amount in the range of 1,000-100,000 ppm based on the total weight of the composition. Preferably, the amount of ascorbate compound added is about equal to the amount of diterpene antioxidant added to the composition.

In Examples 7 and 8 of EVANS it is demonstrated that both carnosic acid and carnosol significantly inhibit the UVB induced formation of lipoperoxides in human skin even at relatively low concentrations (10 ppm), this effect increasing with increasing concentration of carnosic acid and carnosol (see Tables 2 and 3 in column 8 of EVANS).

Example 9 of EVANS demonstrates that UVB radiation gradually decomposes carnosic acid but that through the addition of sodium erythorbate the decomposition of carnosic acid is virtually eliminated, with the sodium erythorbate being decomposed instead.

Accordingly, EVANS teaches and demonstrates that the particular antioxidants disclosed therein, i.e., (pure) carnosic acid and derivatives thereof and the corresponding alcohol, carnosol, are "extremely effective in protecting the skin from peroxidation when applied topically". In view thereof, Appellants are unable to see why one of ordinary skill in the art would be motivated to add another oxidant which exhibits the same effect as the antioxidants of EVANS to the compositions thereof. If the skin protective effect of a composition in accordance with the teaching of EVANS were to be increased, it would apparently be much more convenient to simply increase the concentration of the antioxidants

taught by EVANS (as demonstrated in Examples 7 and 8, the protective effect increases with increasing concentration of the antioxidant(s) taught by EVANS).

EVANS does disclose that it may be advantageous to use an additional antioxidant in the compositions thereof. This additional antioxidant is to protect the active antioxidant of EVANS itself from UV induced degradation. EVANS teaches that for this purpose "ascorbic acid or related compounds such as erythorbic acid, their alkali metal salts" may be used.

In this regard, it is to be noted that in addition to the recommended additional antioxidants EVANS mentions several other compounds which are known for use as antioxidants in cosmetic compositions (see introductory portion in column 1 thereof), i.e., tocopherols, BHA, BHT, hydroquinone and other synthetic compounds. The fact that EVANS does recommend these additional compounds for use in protecting the active ingredients carnosic acid, carnosol, etc. from UV induced degradation can be considered to be a clear indication to one of ordinary skill in the art that even if an additional antioxidant is to be used for protecting the antioxidants of EVANS from UV induced degradation, not each and every compound that is known for use as an antioxidant in cosmetic compositions would be suitable for that purpose.

Moreover, EVANS teaches that the antioxidants which are known for use in cosmetic compositions, while being effective for preventing or retarding spoilage from rancidity (or deterioration from reaction with oxygen) of the compositions themselves, are not effective in protecting the skin which is exposed to UVB radiation from the formation of lipoperoxides, and that only very specific antioxidants such as carnosic acid and carnosol are suitable for the latter purpose (see the passages of EVANS cited above). Accordingly, even if one were to assume, *arguendo*, that one of ordinary skill in the art would be motivated to supplement the

compositions of EVANS by adding thereto an antioxidant which is capable of inhibiting the formation of lipoperoxides in human skin exposed to UVB radiation (i.e., an antioxidant which serves the same purpose at the antioxidants of EVANS) a suitable antioxidant would have to be found first.

2. SUZUKI Fails to Teach or Suggest an Antioxidant which Would Appear Suitable for the Purposes of EVANS

Even if one were to assume, *arguendo*, that one of ordinary skill in the art would be motivated to supplement the compositions of EVANS by an antioxidant which like the antioxidants of EVANS, is capable of inhibiting the formation of lipoperoxides in human skin exposed to UVB radiation, or would be motivated to replace the "ascorbic acid or related compounds such as erythorbic acid, their alkali metal salts" which are taught by EVANS to be capable of protecting the antioxidants taught by EVANS from UV induced decomposition, it is not seen why the compounds of SUZUKI would offer themselves as a good choice for any of these purposes.

Specifically, if one wanted to supplement the compositions of EVANS with an additional antioxidant which is capable of inhibiting the formation of lipoperoxides in human skin exposed to UVB radiation, SUZUKI does not contain any indication that the alpha-glycosylrutin described therein would be a suitable candidate. While SUZUKI appears to indicate that alpha-glycosylrutin is capable of inhibiting the formation of lipoperoxides, SUZUKI fails to teach or suggest that alpha-glycosylrutin is capable of controlling peroxide formation <u>in skin</u>, let alone in skin exposed to sunlight having a harmful intensity of UVB radiation. As set forth above, EVANS clearly indicates that the known antioxidants for use in

cosmetic compositions do not exhibit this particular ability, wherefore there is no reason to assume that each and every antioxidant that is described as suitable for use in a cosmetic composition will automatically be capable of controlling peroxide formation in skin and in particular, in skin that is exposed to sunlight having a harmful intensity of UVB radiation.

Second, if one wanted to replace the "ascorbic acid or related compounds such as erythorbic acid, their alkali metal salts" as agents which are capable of protecting the antioxidants taught by EVANS from UV induced decomposition, SUZUKI again fails to provide any teaching or suggestion that the alpha-glycosylrutin described therein would be a suitable candidate for this purpose.

As set forth above, EVANS indicates that not all of the known antioxidants for use in cosmetic compositions exhibit the ability of protecting carnosic acid, carnosol, etc. from UV induced degradation, wherefore there would be no basis for the assumption that an antioxidant which is described as suitable for use in a cosmetic composition will automatically be capable of protecting the antioxidants of EVANS from UV induced decomposition.

3. A Composition According to EVANS as Modified by SUZUKI Would Not Necessarily be Capable of Treating or Modulating Immunosuppression of Skin Cells Induced by UVB Radiation

Even if one were to assume, *arguendo*, that one of ordinary skill in the art would be motivated to supplement the composition of EVANS with the alpha-glycosylrutin of SUZUKI and to use the corresponding composition for the purpose described in EVANS, i.e., prophylactically against the production of peroxides in skin tissues which have been exposed to sunlight having a harmful intensity of UVB radiation, it is by no means certain that this supplemented composition would contain an amount of alpha-glucosylrutin which is effective

in treating or modulating the immunosuppression of skin cells induced by UVB radiation as recited in, e.g., present claim 37.

In this regard, it needs to be taken into account that the alpha-glycosylrutin of SUZUKI would be incorporated into a composition which already contains one or more antioxidants, i.e. carnosic acid, carnosol etc. and possibly also ascorbic acid, erythorbic acid etc., wherefore one of ordinary skilled in the art would not have any reason to add an amount of alpha-glycosylrutin which is sufficient by itself (i.e., without the additional antioxidant(s) already present in the composition of EVANS) to afford the desired protective effect. In other words, even if one were to assume, *arguendo*, that one of ordinary skill in the art would be motivated to add the alpha-glycosylrutin of SUZUKI to the compositions of EVANS, it would appear likely that the alpha-glycosylrutin would be added in an amount which is smaller than the amount that one would add to a composition which does not contain any other antioxidants. Whether such a reduced amount would still be effective for treating or modulating the immunosuppression of skin cells induced by UVB radiation is not known.

Further, even if one were to assume, *arguendo*, that one of ordinary skill in the art would be motivated to add to the compositions of EVANS an amount of alpha-glycosylrutin which by itself would be effective to protect skin which has been exposed to sunlight having a harmful intensity of UVB radiation from the production of lipoperoxides, it is pointed out that the Examiner has not provided any evidence whatsoever which shows that this amount would automatically also be effective for treating or modulating the immunosuppression of skin cells induced by this UVB radiation.

D. Independent Claim 55 is Not Properly Rejected under 35 U.S.C. § 103(a) as Being Unpatentable Over EVANS in View of SUZUKI as Evidenced by HARRISON and Further in view of N'GUYEN I

Independent claim 55 differs from independent claim 37 discussed in section C. above in that it recites that the cosmetic or dermatological formulation recited therein comprises two additional components (i.e., in addition to one or more flavonoids), i.e., one or more cinnamic acid derivatives and one or more additional antioxidants. In this respect, the rejection essentially asserts that SUZUKI renders it obvious to add alpha-glycosylrutin to the compositions of EVANS and that N'GUYEN teaches that caffeic acid and its esters as well as tocopherols are known to have antioxidant activity, wherefore it would allegedly be obvious to one of ordinary skill in the art to supplement the compositions of EVANS (which are already supplemented by the antioxidant alpha-glycosylrutin of SUZUKI) with caffeic acid and its esters and a further antioxidant such as tocopherol.

Appellants are unable to see what would motivate one of ordinary skill in the art to add to a (merely theoretical) composition which already contains at least two (or even at least three) antioxidants, i.e., (i) carnosic acid, carnosol etc., (ii) alpha-glycosylrutin and, preferably, (iii) ascorbic acid, erythorbic acid etc., two additional antioxidants, i.e., (iv) caffeic acid or an ester thereof and (v) an antioxidant such as tocopherol. In particular, it is not seen that any of the documents cited by the Examiner teaches or suggests that any additional benefit that cannot be achieved by the antioxidants already present in the supplemented composition of EVANS would result from the addition of (at least) two additional antioxidants to this supplemented composition. Appellants note that the Examiner has failed to offer any explanation whatsoever in this regard.

It further is noted that while EVANS acknowledges the use of several types of antioxidants in cosmetic compositions, including tocopherol, this document does not mention, let alone recommend, the use of any of these antioxidants as additional antioxidants for the compositions disclosed therein (with the exception of those which can protect the antioxidants of EVANS from UVB induced decomposition).

E. SUMMARY

To sum up, EVANS in view of SUZUKI neither teaches nor suggests adding alpha-glycosylrutin as an additional antioxidant to the compositions of EVANS. Moreover, even if one were to assume, *arguendo*, that one of ordinary skill in the art would be motivated to add alpha-glycosylrutin to the compositions of EVANS, the Examiner has not provided any evidence which shows that the amount of added alpha-glycosylrutin (alpha-glucosylrutin) would necessarily be efficient for treating or modulating immunomodulation of skin cells induced by UVB radiation.

The Examiner also has failed to explain why one of ordinary skill in the art would be motivated to add two of the antioxidants disclosed by N'GUYEN I to the (theoretical) supplemented composition of EVANS.

Appellants submit that in view of the foregoing, the Examiner has failed to establish a *prima facie* of obviousness of the subject matter of the present independent claims 37 and 55 and the claims dependent therefrom.

F. EVANS in View of SUZUKI as Evidenced by HARRISON Does Not Render Obvious the Subject Matter of Dependent Claim 38

Claim 38, which depends from independent claim 37, recites that immunosuppression is treated. Appellants submit that, even if one were to assume, *arguendo*, that one of ordinary skill in the art would be motivated to supplement a composition according to the teaching of EVANS with the alpha-glycosylrutin of SUZUKI and to use this modified composition for the purpose disclosed by EVANS, i.e., to provide a temporary prophylactic effect against the production of peroxides in skin tissues to which it has been applied (see col. 2, lines 65-67 of EVANS), and even if one were to assume that the modified composition would in theory be capable of treating immunosuppression of skin cells induced by UVB radiation, this would not result in the method of claim 38.

Specifically, since EVANS teaches to use the composition disclosed therein prophylactically, it must be assumed that the composition is applied to skin that has not yet been harmed by UVB rays, wherefore there would be no need to treat the skin. Accordingly, even if one were to assume, *arguendo*, that EVANS in view of SUZUKI as evidenced by HARRISON renders obvious the subject matter of independent claim 37, the Examiner has failed to establish a *prima facie* case of obviousness at least with respect to the subject matter of dependent claim 38.

G. EVANS in View of SUZUKI as Evidenced by HARRISON Does Not Render Obvious the Subject Matter of Dependent Claim 48

Claim 48, which depends from independent claim 37, differs from the latter in that it does not recite alpha-glucosylrutin as a flavonoid which can be comprised in the composition recited in claim 37. Since alpha-glucosylrutin (in the form of alpha-glycosylrutin) is the only flavonoid among the flavonoids recited in claim 37 which is recommended by SUZUKI for incorporation into, *inter alia*, a cosmetic composition (while rutin is also mentioned in SUZUKI, this document points out

that rutin is hardly soluble in water, which renders its practical use very difficult; see, e.g., col. 1, lines 56-59 of SUZUKI), even a combination of the teachings of EVANS and SUZUKI would not result in the composition recited in claim 48.

Accordingly, even if one were to assume, *arguendo*, that EVANS in view of SUZUKI as evidenced by HARRISON renders obvious the subject matter of independent claim 37, the Examiner has failed to establish a *prima facie* case of obviousness at least with respect to the subject matter of dependent claim 48.

H. EVANS in View of SUZUKI as Evidenced by HARRISON and Further in View of N'GUYEN I Does Not Render Obvious the Subject Matter of Dependent Claims 39-42

According to claim 39, which depends from independent claim 37, the composition recited in claim 37 further comprises one or more cinnamic acid derivatives. Claims 40-42 depend from claim 39 either directly or indirectly and recite specific cinnamic acid derivatives. Appellants submit that even if one were to assume, *arguendo*, that one of ordinary skill in the art would be motivated to supplement a composition according to the teaching of EVANS with the alpha-glycosylrutin disclosed by SUZUKI, it is not seen what would motivate one of ordinary skill in the art to add yet another antioxidant to the supplemented composition of EVANS, let alone a cinnamic acid derivative. After all, the supplemented composition would already contain at least two (and preferably at least three) antioxidants, i.e., (i) carnosic acid, carnosol etc., (ii) alpha-glycosylrutin and, preferably, (iii) ascorbic acid, erythorbic acid etc. Appellants fail to see where it is taught or suggested in any of the documents cited by the Examiner that any additional benefit that cannot be achieved by the antioxidants already present in the (theoretical) supplemented composition of EVANS would result from the addition of one or more cinnamic acid derivatives to the

supplemented composition, and neither has the Examiner offered any explanation in this regard.

Accordingly, even if one were to assume, *arguendo*, that EVANS in view of SUZUKI as evidenced by HARRISON renders obvious the subject matter of independent claim 37, the Examiner has failed to establish a *prima facie* case of obviousness at least with respect to the subject matter of dependent claims 39-42.

I. EVANS in View of SUZUKI as Evidenced by HARRISON and Further in View of N'GUYEN I Does Not Render Obvious the Subject Matter of Dependent Claims 51 and 52

Dependent claim 51, which depends from dependent claim 39 (discussed in the preceding section), recites that the weight ratio of the one or more flavonoids of the composition recited in independent claim 37 and the one or more cinnamic acid derivatives recited in claim 39 is from 20 : 1 to 1 : 20. Claim 52, which depends from claim 51, recites that the weight ratio is from 2 : 1 to 1 : 2.

Appellants point out that none of documents cited by the Examiner appears to teach or suggest that any flavonoid and a cinnamic acid derivative should be employed in a certain weight ratio, let alone in a weight ratio range as recited in present claims 51 and 52, and neither has the Examiner pointed to any passages of the cited documents which would appear to render it obvious to one or ordinary skill in the art to provide a flavonoid and a cinnamic acid derivative in the weight ratio ranges of claims 51 and 52.

Accordingly, even if one were to assume, *arguendo*, that EVANS in view of SUZUKI as evidenced by HARRISON renders obvious the subject matter of independent claim 37, the Examiner has failed to establish a *prima facie* case of obviousness at least with respect to the subject matter of dependent claims 51 and 52.

J. EVANS in View of SUZUKI as Evidenced by HARRISON and Further in View of N'GUYEN I Does Not Render Obvious the Subject Matter of Dependent Claim 56

According to claim 56, which depends from claim 55, the one or more antioxidants which are present in the composition recited in claim 55 in addition to the one or more flavonoids and one or more hydroxycinnamic acid derivatives comprise at least one of a tocopherol and a derivative thereof.

In this regard, the Examiner relies on N'GUYEN and alleges that this document teaches that caffeic acid and its esters as well as tocopherols are known to have antioxidant activity and essentially asserts that in view thereof, one or ordinary skill in the art would have been motivated to add caffeic acid and its esters and another oxidant such as tocopherol to the supplemented compositions of EVANS.

Appellants submit that even if it were assumed, *arguendo*, that one of ordinary skill in the art would be motivated by N'GUYEN I to add caffeic acid and its esters and another oxidant to the supplemented compositions of EVANS, this other oxidant would not be a tocopherol.

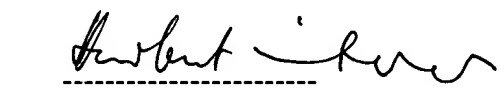
Specifically, according to col. 2, lines 53-57 of N'GUYEN I, the antioxidant system disclosed therein comprises, *inter alia*, 0.5 to 20 weight percent of tocopherol or caffeic acid. In other words, according to N'GUYEN I, tocopherol and caffeic acid are alternatives. This is confirmed by the compositions described in the Examples of N'GUYEN I, most of which contain either tocopherols (Examples 4-6, 10, 11, I-III, VII and VIII) or caffeic acid (Examples 7-9, IV-VI), but none of them contains both tocopherols and caffeic acid. Accordingly, neither N'GUYEN I nor any of the other documents cited by the Examiner teaches or suggests employing caffeic acid and a tocopherol in combination.

Accordingly, even if one were to assume, *arguendo*, that EVANS in view of SUZUKI as evidenced by HARRISON and further in view of N'GUYEN I renders obvious the subject matter of independent claim 55, the Examiner has failed to establish a *prima facie* case of obviousness at least with respect to the subject matter of dependent claim 56.

VIII. CONCLUSION

Appellants respectfully submit that for at least all of the foregoing reasons, the Examiner has failed to establish a *prima facie* case of obviousness of the subject matter of any one of present claims 37-56 with respect to EVANS in view of SUZUKI and further in view of N'GUYEN I or N'GUYEN II as evidenced by HARRISON, which is a prerequisite for maintaining a rejection under 35 U.S.C. § 103. The Board is, therefore, respectfully requested to reverse the Final Rejection and to allow the application to issue in its present form.

Respectfully submitted,
Ghita LANZENDORFER et al.



Neil F. Greenblum
Reg. No. 28,394

January 29, 2007
GREENBLUM & BERNSTEIN, P.L.C.
1950 Roland Clarke Place
Reston, VA 20191
(703) 716-1191

Heribert F. Muensterer
Reg. No. 50,417

CLAIMS APPENDIX

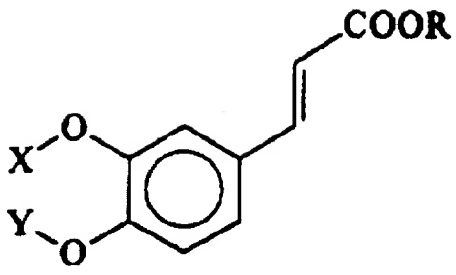
37. A method of treating or modulating immunosuppression of skin cells induced by UVB radiation, wherein the method comprises topically applying to the skin of a person in need thereof an effective amount therefor of a cosmetic or dermatological formulation comprising one or more flavonoids selected from alpha-glucosylrutin, alpha-glucosylmyricitrin, alpha-glucosylquercitrinin, alpha-glucosylquercitrin, quercetin, rutin, chrysin, kaempferol, myricetin, rhamnetin, apigenin, luteolin, naringin, hesperidin, naringenin, hesperitin, morin, phloridzin, diosmin, fisetin, vitexin, neohesperidin, dihydrochalcone, flavone and genistein and wherein immunosuppression of skin cells induced by UVB radiation is treated or modulated.

38. The method of claim 37, wherein immunosuppression is treated.

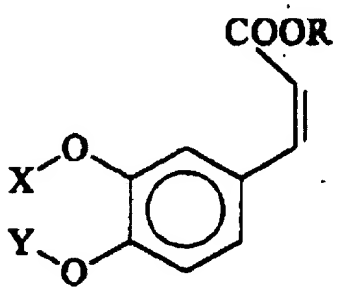
39. The method of claim 37, wherein the composition further comprises one or more cinnamic acid derivatives.

40. The method of claim 39, wherein the one or more cinnamic acid derivatives comprise one or more hydroxycinnamic acid derivatives.

41. The method of claim 40, wherein the one or more hydroxycinnamic acid derivatives comprise at least one of a compound of formula



and a compound of formula



wherein X and Y independently represent H or an unbranched or branched alkyl group having from 1 to 18 carbon atoms.

42. The method of claim 40, wherein the one or more hydroxycinnamic acid derivatives comprise at least one of caffeic acid and ferulic acid.

43. The method of claim 37, wherein the composition further comprises one or more antioxidants.

44. The method of claim 39, wherein the composition further comprises one or more antioxidants.

45. The method of claim 41, wherein the composition further comprises one or more antioxidants.

46. The method of claim 43, wherein the one or more antioxidants comprise at least one of a tocopherol and a derivative thereof.

47. The method of claim 45, wherein the one or more antioxidants comprise at least one of a tocopherol and a derivative thereof.

48. The method of claim 37, wherein the cosmetic or dermatological formulation comprises one or more of alpha-glucosylmyricitrin, alpha-glucosylquercitrinin, alpha-glucosylquercitrin, rutin, chrysin, kaempferol, myricetin, rhamnetin, apigenin, luteolin, naringin, hesperidin, naringenin, hesperitin, morin, phloridzin, diosmin, fisetin, vitexin, neohesperidin, dihydrochalcone, flavone and genistein.

49. The method of claim 37, wherein the cosmetic or dermatological formulation comprises from 0.01 % to 10 % by weight of the one or more flavonoids, based on a total weight of the formulation.

50. The method of claim 49, wherein the cosmetic or dermatological formulation comprises from 0.1 % to 6 % by weight of the one or more flavonoids.

51. The method of claim 39, wherein a weight ratio of the one or more flavonoids and the one

or more cinnamic acid derivatives is from 20 : 1 to 1 : 20.

52. The method of claim 51, wherein the weight ratio is from 2 : 1 to 1 : 2.

53. The method of claim 37, wherein the cosmetic or dermatological formulation comprises an emulsion.

54. The method of claim 37, wherein the cosmetic or dermatological formulation comprises a gel.

55. A method of treating immunosuppression of skin cells induced by UVB radiation, wherein the method comprises topically applying to the skin of a person in need thereof an effective amount therefor of a cosmetic or dermatological formulation comprising (i) one or more flavonoids selected from alpha-glucosylrutin, alpha-glucosylmyricitrin, alpha-glucosylquercitrinin, alpha-glucosylquercitrin, quercetin, rutin, chrysin, kaempferol, myricetin, rhamnetin, apigenin, luteolin, naringin, hesperidin, naringenin, hesperitin, morin, phloridzin, diosmin, fisetin, vitexin, neohesperidin, dihydrochalcone, flavone and genistein, (ii) one or more cinnamic acid derivatives and (iii) one or more antioxidants, and wherein immunosuppression of skin cells induced by UVB radiation is treated.

56. The method of claim 55, wherein the one one more cinnamic acid derivatives comprise at least one hydroxycinnamic acid derivative and wherein the one or more antioxidants comprise at least one of a tocopherol and a derivative thereof.

EVIDENCE APPENDIX

None.

P29690.A08

RELATED PROCEEDINGS APPENDIX

None.